P330



# Out of the warm little pond: prerequisites for an evolvable system

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> But if (and oh! what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, &c., present, that a protein compound was chemically formed ready to undergo still more complex changes. [1]

At the outset of my scientific career around 60 years ago, biology faced three major challenges: (1) the nature of genetic systems, and how they played out the evolutionary drama; (2) the development of the organism under instruction from the genetic blueprints, including ultimately the central nervous system and its psychological manifestations; and (3) the ultimate historical origin of these systems, an explanation of the transition from inanimate chemistry to evolving, metabolizing, developing organisms. To borrow a coinage from N.W. Pirie, I call this 'eobiology'.

The first two challenges are now thriving enterprises, greatly enriched by the molecularization of biology, the rooting of genetics and of epigenesis in the chemistry of DNA, RNA and proteins. This special issue of *Endeavour* on the history of heredity reveals fascinating insights into how humankind has dealt with these two challenges. But, as far as the third challenge, eobiology, is concerned, we would do well to acknowledge its vastness. A web search for 'origin of life' generates more than 80 000 hits, with citations to Oparin (for his seminal *Origin of Life*) in the thousands; but there is no persuasive consensus. I will offer only an idiosyncratic glimpse, gleaned over decades of observation.

Nevertheless, eobiology has surmounted some stumbling blocks: it was hard to envisage the simultaneous emergence of self-replicating templates (DNA) and the parallel protein enzymatic apparatus needed to support that. The discovery of ribozymy, that RNA could be both a template and a catalyst, engendered images of an RNA world that preceded DNA and protein. But, there remains a huge gap between Darwin's 'warm little pond' and the microwell laden with RNA precursors that might be envisaged as the primordial RNA. Arguably, ribonucleotides do self-assemble on clay and might by chance generate template-competent RNAs [2]; for this and many other postulated initial reactions, the pace available to natural evolution may be a billion-fold slower than our assays can measure: patience may be the ultimate limiting factor for simulation. Thus, the canonical story for the origin of life on earth has tended to invoke a terrestrial venue for primitive organic molecules, and a belief that these would somehow transcend the thresholds needed to initialize an autocatalytic RNA ensemble.

However, the venue for eobiochemistry might, but need not, be earthbound. In 1953, Stanley Miller and Harold Urey had famously demonstrated the production of amino acids from irradiated atmospheric gases, substantiating at least part of Darwin's vision. But, as I argued in 1958 [3], there was room for a larger perspective. After hydrogen and helium, the most abundant elements in the cosmos are C, O and N. The interstellar gas could not possibly have condensed to form stars and planetary systems without an enormous intervening anabolism of these elements into molecular species; it was just that few astronomers spoke organic chemistry in those days. Compared to massive planets such as Jupiter, comets and interstellar space, earth was grossly depleted of these elementary units, which had largely been blown away by the solar wind. Even earth's surface, Tommy Gold argues, is largely bereft of organic elements compared to the ongoing effusion from deeper layers of primitive methane and other molecules, relics of its original condensation. His 'deep hot biosphere' is a comet under our feet.

Since 1958, the emergence of molecular cosmology has yielded abundant spectroscopic evidence for a host of organic molecules in the reaches of outer space [4]. Indeed, carbonaceous grains would nucleate and hence hasten the agglomeration of disperse plasmas in star formation, bringing us closer to an eobiological and cosmological synthesis. There might even be a primitive natural selection for grain conformations that were fissile, and hence prone to amplifying the numbers of nuclei. And what might have preceded RNA as an information molecule? Primitive condensates of 'HCON' offer a wide range of polymerizable monomers in abundant yield. As with our synthetic plastics, they might engender polyesters, polyethers and polypeptides, not at all excluding mixed polymers. Can any of these polymers offer template-directed assembly? Hardly any experiments have been attempted, but there is at least one lead. Lee *et al.* [5] illustrate such a principle with ligation of oligopeptides. This advance may well encourage more experimentation towards assemblies that tend to extract one monomer at a time, preferentially, from a feasible soup. That is all we need ask of an evolvable system [6].

**References**

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